UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/654,328	09/01/2000	Michael B. Brenner	B0801/7187(ERP/MAT)	5793

7590 12/15/2003

Elizabeth R Plumer
Wolf Greenfield & Sacks P C
600 Altantic Avenue
Boston, MA 02210

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/654,328	BRENNER ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,6,16,44,45 and 50-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,6,16,44,45 and 50-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1, 3, 5-6, 16, 44-45 and 50-58 are pending and under consideration in the instant application.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/16/2003 has been entered.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 3, 5, 6, 16, 44-45 and 50-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating a subject having a an inflammatory joint disorder comprising administering locally to a synovium of the subject an anti cadherin-11 antibody provided applicant provides support as how to extrapolate data obtained from *in vitro* assay to the development of effective *in vivo* human therapeutic methods as presented in the previous Office Action. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or the invention commensurate in scope with these claims essentially for the same reasons set forth in the previous Office Actions mailed 4/26/02 and 1/14/03.

Applicant submits that the previously submitted data were generated by experiments conducted in accordance with the teaching in the specification and thus they establish that the specification is enabling as of the time of filing. Applicant contends that the data demonstrate that administration of cadherin-11-Fc fusion protein to mice having serum-induced arthritis caused reduction in clinical symptoms of inflammatory arthritis including reduced ankle thickness, delay in arthritis onset, and decreased maximal arthritic index. Applicant concludes such data confirm the teaching in the specification that inhibition of cadherin-11 binding (whether by cadherin-11-Fc fusion protein or anti-cadherin-11 antibody) ameliorates inflammatory arthritis, as shown in a murine arthritis model. Applicant further addresses the Examiner's concern regarding the active immunization issue of the cadherin-11-Fc fusion protein. Applicant asserts that the administration of cadherin-11-Fc-fusion protein does not trigger antibody production as provided in the Dr. Brenner Declaration. Applicant asserts that the Declaration data supports the involvement of passive rather than active immunotherapy as the mechanism of action of the cadherin-11-Fc protein. (1) the cadherin-11-Fc fusion protein is structurally analogous to an anti-cadherin-11 antibody. It contains an Fc domain as well as "an antigen biding domain", the extracellular domain of cadherin-11 protein. The cadherin-11-Fc fusion also possesses "two

antigen binding domains" as does an anti-cadherin-11 antibody. (2) the binding activities of the cadherin-11-Fc fusion protein and the anti-cadherin-11 antibody are similar that is both agents will bind to Fc receptors and to cadherin-11 molecules. (3) the response kinetics in the previously submitted data are consistent with passive by not active immunization. The data show that clinical activity was observed with co-administration of the cadherin-11-Fc fusion protein and arthritis inducing serum. (4) the cadherin-11 –Fc fusion proteins administered to the murine subjects were of mouse origin and thus would not be expected to elicit an antibody response.

While Dr. Brenner's Declaration provides some data to show that cadherin-11-Fc fusion protein involve in a passive immunotherapy in a similar way the antibody treatment would work. However, the cadherin-11-Fc fusion protein and anti-cadherin-11 antibodies are structurally and functionally distinct. Fusion protein and antibodies differ with respect to their structure, physiochemical properties, and modes of action. Further, peptides bind differently to cadherin-11 than anti-cadherin-11antibodies bind to cadherin-11, which leads to key interactions that impact binding kinetics. It is well known that peptides exhibit lower binding affinity than their antibody counterpart. Thus faced with the use of structurally distinct cadherin-11-Fc-fusion protein in a method of treating rheumatoid arthritis, undue experimentation would be required of the skilled artisan to determine the effect of anti-cadherin-11 antibodies on rheumatoid arthritis *in vivo* in view of the instant disclosure.

5. The declaration by Dr. Brenner under 37 CFR 1.132 filed 7/16/03 is insufficient to overcome the rejection based upon 35 U.S.C. 112, first paragraph as set forth in the previous Office actions because while the data show that cadherin-11-Fc fusion protein involve in a passive immunotherapy in a similar way the antibody treatment would work, peptides bind differently to cadherin-11 than anti-cadherin-11antibodies bind to cadherin-11, which leads to key interactions that impact binding kinetics. Regarding the correlation of rheumatoid arthritis and inflammatory joint disease, Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. Therefore, absent the ability to predict which of these disease would be treated as claimed, and given the lack of data on a particular disease, for one of skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
November 28, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600